

PATENT ABSTRACTS OF JAPAN

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(54) SURFACE PLASMON RESONANCE MEASURING APPARATUS

(57)Abstract:

PROBLEM TO BE SOLVED: To allow a surface plasmon resonance measuring apparatus to obtain a light detection signal with a high S/N even if light beams are caused to impinge on the interface between a dielectric block and a metallic film while their incident angle is fixed.

SOLUTION: The surface plasmon resonance measuring apparatus comprises dielectric blocks 11 and 13; a metallic film 14 formed on one side of each of the dielectric blocks 11 and 13 and brought into contact with a sample 15; light sources 16 and 17 emitting two or more light beams L1 and L2 with different wavelengths; and an incident optical system 18 meeting the requirement for total reflection at the interface 13a between each of the blocks 11 and 13 and the metallic film 14 and causing the beams to impinge at the same position on the interface 13a at the fixed incident angle included in the requirement for surface plasmon resonance. The strength of the light beam L totally reflected by the interface 13a is measured by light detection means 21 and 22 for each wavelength, and light detection signals S1 and S2 as to the two light beams L1 and L2 with different wavelengths, outputted by the light detection means 21 and 22, are input to a computing means 23 to calculate their difference.

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**CLAIMS**

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[Claim(s)]

[Claim 1]A surface plasmon resonance measuring device comprising:

A dielectric block.

A metal membrane which is formed in the whole surface of this dielectric block, and is contacted in a sample.

A light source which emits an optical beam of two or more mutually different wavelength.

An optical beam of said two or more wavelength to an interface of said dielectric block and a metal membrane by a fixed incidence angle from which a total reflection condition is acquired. A calculating means which asks for difference of a photodetection signal about an optical beam of two mutually different wavelength which an incident light study system in which the same position of said interface is entered from the dielectric block side, a photodetection means which measures intensity of an optical beam which carried out total internal reflection by said interface for every wavelength, and this photodetection means output.

[Claim 2]Said light source is what emits an optical beam of three or more mutually different wavelength, The surface plasmon resonance measuring device according to claim 1, wherein said calculating means is constituted so that it may ask for difference of a photodetection signal about an optical beam of two wavelength which fulfills surface-plasmon-resonance conditions among those wavelength.

[Claim 3]A means to separate spectrally an optical beam after it is constituted so that said incident light study system may multiplex to one and may lead an optical beam of said two or more wavelength to the same position of said interface, and said photodetection means carries out total internal reflection by said interface for every

wavelength, The surface plasmon resonance measuring device according to claim 1 or 2 comprising two or more photodetectors which measure intensity of an optical beam separated spectrally individually, respectively.

[Claim 4] Said light source mutually an optical beam of said two or more wavelength by constituting a time interval so that it may set and eject, and carrying out detecting operation to timing to which said photodetection means synchronized with optical beam ejection timing of said light source, The surface plasmon resonance measuring device according to claim 1 or 2 comprising one photodetector which measures intensity of said optical beam for every wavelength.

[Claim 5] Said incident light study system is constituted so that it may irradiate with a two-dimensional field in said interface by said optical beam, A surface plasmon resonance measuring device given [ claim 1, wherein said photodetection means comprises a two-dimensional photodetector which detects intensity of an optical beam which carried out total internal reflection by said interface for every position in said two-dimensional field to ] in 4 any 1 paragraphs.

[Claim 6] A surface plasmon resonance measuring device given [ claim 1, wherein a sensing medium which produces a specific component and an interaction in a sample on the surface of said metal membrane is arranged to ] in 5 any 1 paragraphs.

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## **DETAILED DESCRIPTION**

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[Detailed Description of the Invention]

[0001]

[Field of the Invention] This invention relates to the surface plasmon resonance measuring device which carries out the quantitative analysis of the substance in a sample using generating of surface plasmon.

[0002]

[Description of the Prior Art] The compressional wave which a free electron vibrates collectively and is called a plasma wave into metal arises. And what quantized this compressional wave produced in a surface of metal is called surface plasmon.

[0003] Conventionally, the surface plasmon resonance measuring device which carries out the quantitative analysis of the substance in a sample is variously proposed using the phenomenon in which this surface plasmon is excited by the light wave. And the thing using the system called Kretschmann arrangement as what is especially known well in them is mentioned (for example, refer to JP,6-167443,A).

[0004] The dielectric block in which the surface plasmon resonance measuring device using the above-mentioned system was fundamentally formed, for example in the shape of prism, The metal membrane which is formed in the whole surface of this dielectric

block, and is contacted in a sample, A dielectric block is received in the light source made to generate an optical beam and the above-mentioned optical beam, The incident light study system entered so that various incidence angles which serve as a total reflection condition by the interface of this dielectric block and a metal membrane, and include surface-plasmon-resonance conditions may be acquired, It has a photodetection means which measures the intensity of the optical beam which carried out total internal reflection by the above-mentioned interface, and detects the state of surface plasmon resonance.

[0005]In order to acquire various incidence angles as mentioned above, a comparatively thick optical beam may be entered so that it may converge by the above-mentioned interface, so that the ingredient which may deflect a comparatively thin optical beam, and may enter the above-mentioned interface, or enters into an optical beam at an angle of versatility may be contained. In the case of the former, the small photodetector which carries out a synchronized drive to the deviation of an optical beam can detect the optical beam from which an angle of reflection changes with the deviation of an optical beam, or it can detect it by the area sensor prolonged along the change direction of an angle of reflection. On the other hand, in the case of the latter, it is detectable by the area sensor prolonged in the direction which can receive the whole of each optical beam reflected by various angles of reflection.

[0006]In the surface plasmon resonance measuring device of the above-mentioned composition, if an optical beam is entered by specific incidence angle  $\theta_{sp}$  beyond a total reflection angle to a metal membrane, The evanescent wave which has electric field distribution in the sample which is in contact with this metal membrane arises, and surface plasmon is excited by the interface of a metal membrane and a sample by this evanescent wave. When the wave number vector of evanescent light is equal to the wave number of surface plasmon and wave number consistency is materialized, since it will be in a resonance state and luminous energy shifts to surface plasmon, the luminous intensity which carried out total internal reflection by the interface of a dielectric block and a metal membrane decreases both keenly. Generally attenuation of this light intensity is detected as a dark line by the above-mentioned photodetection means.

[0007]The incidence angle  $\theta$  at the time of this total-reflection-attenuation phenomenon arising and the relation with the reflected light intensity  $I$  are roughly shown in drawing 5. Incidence angle  $\theta_{sp}$  shown here is an incidence angle which above-mentioned total reflection attenuation (ATR) produces.

[0008]The above-mentioned resonance is produced only when an incident beam is p-polarized light. Therefore, it is necessary to set up beforehand so that an optical beam may enter by p-polarized light.

[0009]If incidence angle  $\theta_{sp}$  which this total reflection attenuation (ATR) produces shows the wave number of surface plasmon, the dielectric constant of a sample will be called for. That is, about the wave number of surface plasmon, when angular frequency

of  $K_{SP}$  and surface plasmon is set to  $\omega$  and the velocity of light,  $\epsilon_{m}$ , and  $\epsilon_s$  in a vacuum are made into the dielectric constant of metal and a sample for  $c$ , respectively, there are the following relations.

[0010]

[Equation 1]

$$K_{SP}(\omega) = \frac{\omega}{c} \sqrt{\frac{\epsilon_m(\omega) \epsilon_s}{\epsilon_m(\omega) + \epsilon_s}}$$

Since the concentration of the special material in a sample is known based on a predetermined calibration curve etc. if dielectric constant  $\epsilon_s$  of a sample is known, the quantitative analysis of the special material in a sample can be carried out by getting to know incidence angle  $\theta_{SP}$  to which the above-mentioned reflected light intensity falls after all.

[0011] In an above-mentioned surface plasmon resonance measuring device, While constituting said incident light study system so that an optical beam may irradiate with the two-dimensional field in the interface of a dielectric block and a metal membrane, By using what consists of a two-dimensional photodetector which detects the intensity of the optical beam which carried out total internal reflection by the above-mentioned interface for every position in the above-mentioned two-dimensional field as said photodetection means, Since the dielectric constant distribution in this field of the sample arranged corresponding to the above-mentioned two-dimensional field is searched for, based on it, the concentration distribution of the special material in a sample can be searched for.

[0012] About the surface plasmon resonance measuring device which makes the two-dimensional field in the interface of a dielectric block and a metal membrane irradiate with an optical beam, an example is shown in NATURE Vol.332, 14, and APRIL 1988 pp.615-617 in this way.

[0013]

[Problem(s) to be Solved by the Invention] By the way, in this surface plasmon resonance measuring device, especially when searching for the concentration distribution of the special material in a sample using the above-mentioned two-dimensional photodetector, the incidence angle of the optical beam to the interface of a dielectric block and a metal membrane will be fixed, but. In that case, the fault that S/N of a photodetection signal is not good is accepted.

[0014] An object of this invention is to provide the surface plasmon resonance measuring device which can acquire the photodetection signal of high S/N also as immobilization for the incidence angle of an optical beam in light of the above-mentioned circumstances.

[0015]

[Means for Solving the Problem]A surface plasmon resonance measuring device by this invention, A dielectric block which was mentioned above, a metal membrane, and a light source which emits an optical beam, In a surface plasmon resonance measuring device provided with an incident light study system in which this optical beam is entered from the dielectric block side to an interface of said dielectric block and a metal membrane by a fixed incidence angle from which a total reflection condition is acquired, and a photodetection means, After what emits an optical beam of two or more mutually different wavelength was used and a measurable thing is used for every wavelength as a photodetection means as the above-mentioned light source in intensity of an optical beam which carried out total internal reflection by an interface of a dielectric block and a metal membrane, A calculating means which asks for difference of a photodetection signal about an optical beam of two mutually different wavelength which this photodetection means outputs was established.

[0016]In a surface plasmon resonance measuring device of this invention which has the above-mentioned composition, After what emits an optical beam of three or more mutually different wavelength as said light source is applied, it is desirable to constitute said calculating means so that it may ask for difference of a photodetection signal about an optical beam of two wavelength which fulfills surface-plasmon-resonance conditions among those wavelength.

[0017]In a surface plasmon resonance measuring device of this invention, A means to separate spectrally an optical beam in which a photodetection means carried out total internal reflection by said interface for every wavelength while it is constituted so that an incident light study system may multiplex to one and may lead an optical beam of two or more wavelength to the same position of said interface, It is desirable to comprise two or more photodetectors which measure intensity of an optical beam separated spectrally individually, respectively.

[0018]Or after being constituted instead of adopting composition using such two or more photodetectors so that a light source may set and eject an optical beam of two or more wavelength for a time interval mutually, A photodetection means may comprise one photodetector which measures intensity of an optical beam for every wavelength by carrying out detecting operation to optical beam ejection timing of a light source, and timing which synchronized.

[0019]In this case, two or more light sources of each other which emit an optical beam of each wavelength are fixed to a separate position, It may constitute so that an optical beam respectively emitted from them may follow the same optical path mutually from the middle by dichroic mirror or other means (not multiplexed since it dissociates in time). Or at the time of lighting, it is made to move to a common position which serves as predetermined relative position relation to an incident light study system, and may be made to carry out lighting operation of the light source of these plurality in the position.

[0020]In a surface plasmon resonance measuring device of this invention, While an

incident light study system is constituted so that it may irradiate with a two-dimensional field in said interface by an optical beam, it is desirable for a photodetection means to comprise a two-dimensional photodetector which detects intensity of an optical beam which carried out total internal reflection by said interface for every position in said two-dimensional field.

[0021]In a surface plasmon resonance measuring device of this invention, it is still more desirable to arrange a sensing medium which produces a specific component and an interaction in a sample on the surface of said metal membrane.

[0022]

[Effect of the Invention]The relation between the wavelength of the optical beam in the surface plasmon resonance measuring device of this invention and the intensity (it corresponds to the detected total-internal-reflection luminous intensity) of the photodetection signal which a photodetection means outputs is shown in drawing 6. That the evanescent light mentioned above and surface plasmon resonate, Since it is a case where the wave number vector of this evanescent light is equal to the wave number of surface plasmon, and wave number consistency is materialized, if the wavelength of the optical beam in which the interface of a dielectric block and a metal membrane is entered is changed, Total-internal-reflection light intensity changes like the case where the incidence angle  $\theta$  of the optical beam to this interface is changed. That is, in the case of the characteristic of the curve a, when the wavelength of an optical beam is  $\lambda_{sp}$ , total reflection attenuation arises, for example.

[0023]And if the relation of this wavelength versus total-internal-reflection light intensity fixes the above-mentioned incidence angle  $\theta$ , as the curves a and b show to drawing 6, it will change according to the concentration of the special material in a sample, corresponding [ that is, ] to dielectric constant  $\epsilon_s$  of a sample. Then, considering the case where the wavelength of an optical beam is  $\lambda_1$  and  $\lambda_2$ , the difference of the photodetection signal about the light of the wavelength  $\lambda_1$  and the photodetection signal about the light of the wavelength  $\lambda_2$  will change according to the concentration of the above-mentioned special material. That is, for example to the difference in the case of the curve a being (S1 a-S 2a), the difference in the case of the curve b serves as (S1 b-S2b), and both values differ clearly.

[0024]Therefore, if the analytical curve for every sample for which it has asked beforehand, etc. are referred to, based on this difference, presumption of the relation of wavelength versus total-internal-reflection light intensity will be attained, and it will come carry out the quantitative analysis of the special material in a sample.

[0025]And since the noise component which had ridden on each signal will be offset if it asks for the difference of two photodetection signals as mentioned above, S/N will become high enough and this differential signal can carry out the quantitative analysis of special material with high degree of accuracy based on this differential signal.

[0026]After what emits the optical beam of three or more mutually different wavelength

especially as said light source among the surface plasmon resonance measuring devices of this invention is used, In what was constituted so that said calculating means might ask for the difference of the photodetection signal about the optical beam of two wavelength which fulfills surface-plasmon-resonance conditions among those wavelength, Since it becomes easy to secure two another wavelength which fulfills surface-plasmon-resonance conditions even if it seems that a certain wavelength may have separated from surface-plasmon-resonance conditions by preparing three or more wavelength, correspondence in various samples is attained.

[0027]Among the surface plasmon resonance measuring devices of this invention, especially an incident light study system, While it is constituted so that it may irradiate with the two-dimensional field in said interface by an optical beam, In what comprised a two-dimensional photodetector which detects the intensity of the optical beam in which the photodetection means carried out total internal reflection by the above-mentioned interface for every position in the above-mentioned two-dimensional field, Since a differential signal is searched for for every position in the above-mentioned two-dimensional field, it becomes possible to search for the concentration distribution of the special material in this field, etc. based on this differential signal.

[0028]In what arranged the sensing medium which produces the specific component and interaction in a sample especially on the surface of a metal membrane among the surface plasmon resonance measuring devices of this invention, Since the state of surface plasmon resonance changes with above-mentioned interactions when a sample is made to hold on this sensing medium, the specific reaction of the specific component in a sample and a sensing medium is detectable by catching this change.

[0029]

[Embodiment of the Invention]Hereafter, with reference to drawings, an embodiment of the invention is described in detail. Drawing 1 shows the outline side shape of the surface plasmon resonance measuring device by a 1st embodiment of this invention.

[0030]This surface plasmon resonance measuring device is provided with the following as a graphic display.

For example, transparent dielectric prism 11 formed in trianglepole shape.

The transparent dielectric plate 13 fixed to the upper surface of this dielectric prism 11 via the refractive-index matching liquid 12.

The metal thin film 14 which consists of gold, silver, copper, aluminum, etc. for example, it was formed in the upper surface of this dielectric plate 13.

And the sample 15 of an analysis object is arranged on this metal thin film 14. According to this embodiment, the dielectric block is formed with the transparent dielectric prism 11, the refractive-index matching liquid 12, and the transparent dielectric plate 13.

[0031]It is provided by the 1st laser light source 16 that emits the optical beam L1 of the wavelength  $\lambda_1$ , and the 2nd laser light source 17 that emits the optical beam L2



of the wavelength  $\lambda_2$ , and these optical beams L1 and L2, It is multiplexed by one optical beam L with the dichroic mirror 18 as an incident light study system which makes the former penetrate and in which the latter is reflected. This optical beam L it was multiplexed [ L ] enters into the dielectric prism 11 in the state of a thin parallel beam, and enters into the interface 13a of the dielectric plate 13 and the metal thin film 14. Let the incidence angle  $\theta$  at this time be a value within the limits which the total reflection condition of optical beam L is acquired in the above-mentioned interface 13a, and surface plasmon resonance may produce.

[0032]Optical beam L needs to enter by p-polarized light to the interface 13a. What is necessary is just to allocate the 1st laser light source 16 and 2nd laser light source 17 beforehand so that the polarization direction of the optical beams L1 and L2 may turn into a determined direction in order to make it such. In addition, direction of the optical beam L1 and polarization of L2 may be controlled by the wavelength plate or a polarizing plate.

[0033]On the other hand, the light of the wavelength  $\lambda_2$  is separated spectrally into the optical beam L1 of the wavelength  $\lambda_1$ , and the optical beam L2 of the wavelength  $\lambda_2$  with the dichroic mirror 20 which carries out total internal reflection of the optical beam L which entered into the interface 13a there, in which optical beam L which carried out total internal reflection makes the light of the wavelength  $\lambda_1$  penetrate and to reflect. The optical beam L1 and the optical beam L2 are detected by the 1st photodetector 21 and the 2nd photodetector 22 which consist of photo-diodes etc., respectively.

[0034]Both the photodetection signal S1 which the 1st photodetector 21 outputs, and the photodetection signal S2 which the 2nd photodetector 22 outputs are inputted into the difference calculation circuit 23. This difference calculation circuit 23 asks for difference with the inputted photodetection signals S1 and S2, and outputs the differential signal Ss.

[0035]Hereafter, the sample analyzing by the surface plasmon resonance measuring device of the above-mentioned composition is explained. The sample 15 with which analysis is presented is allotted on the metal thin film 14. And the laser light sources 16 and 17 drive, it is multiplexed in the optical beams L1 and L2 respectively emitted from them with the dichroic mirror 18, and optical beam L it was multiplexed [ L ] enters into the interface 13a of the dielectric plate 13 and the metal thin film 14 by the fixed incidence angle  $\theta$ . Since this incidence angle  $\theta$  is set up as above-mentioned, it carries out total internal reflection of the optical beam L by the interface 13a.

[0036]Thus, when optical beam L carries out total internal reflection, an evanescent wave oozes out from the interface 13a to the metal thin film 14 side. When the incidence angle  $\theta$  is being fixed, total-internal-reflection luminous intensity (that is, the photodetection signal S1 which the photodetectors 21 and 22 output, the intensity of S2) changes, as are mentioned above, and shown in drawing 6 according to the light

wavelength  $\lambda$ . That is, since the above-mentioned evanescent wave resonates with the surface plasmon excited on the surface of the metal thin film 14 when the light wavelength  $\lambda$  is  $\lambda_{sp}$ , about the light of this wavelength  $\lambda_{sp}$ , reflected light intensity declines keenly.

[0037]And if the incidence angle  $\theta$  is being fixed, the relation of this wavelength versus total-internal-reflection light intensity will change according to the concentration of the special material in a sample, corresponding [ that is, ] to dielectric constant  $\epsilon_s$  of a sample, as the curves a and b show to drawing 6. Then, the value of the photodetection signal S1 and the differential signal Ss which took the difference of S2 will change according to the concentration of the above-mentioned special material. Therefore, if the analytical curve for every sample for which it has asked beforehand, etc. are referred to, based on the value of this differential signal Ss, presumption of the relation of wavelength versus total-internal-reflection light intensity will be attained, and the quantitative analysis of the special material in the sample 15 will be carried out.

[0038]And since each signal S1 and the noise component which had ridden on S2 will be offset if it asks for the two photodetection signals S1 and the difference of S2 as mentioned above, S/N will become high enough and the differential signal Ss can carry out the quantitative analysis of special material with high degree of accuracy based on this differential signal Ss.

[0039]Next, a 2nd embodiment of this invention is described with reference to drawing 2. Drawing 2 shows the outline side shape of the surface plasmon resonance measuring device of this 2nd embodiment. In this drawing 2, a jack per line is given to an element equivalent to the element in drawing 1, and especially the explanation about them is omitted, as long as there is no necessity (following, the same).

[0040]In the surface plasmon resonance measuring device of this 2nd embodiment, The drive of the 1st laser light source 16 and the 2nd laser light source 17 is controlled by the drive control circuit 25, after the 1st laser light source 16 carries out a predetermined time drive and stops, a time interval is set and the 2nd laser light source 17 drives. Thereby, after the optical beam L1 of the wavelength  $\lambda_1$  enters into the interface 13a of the dielectric plate 13 and the metal thin film 14, a time interval is set and the optical beam L2 of the wavelength  $\lambda_2$  enters into this interface 13a.

[0041]On the other hand, only the 1st photodetector 21 is formed as a photodetection means, and operation of this photodetector 21 is also controlled by the above-mentioned drive control circuit 25. Namely, when the 1st laser light source 16 drives this photodetector 21, And when the 2nd laser light source 17 drives, detecting operation of the synchronization is taken and carried out, the photodetection signal S1 about the optical beam L1 of the wavelength  $\lambda_1$  is outputted first, and, subsequently the photodetection signal S2 about the optical beam L2 of the wavelength  $\lambda_2$  is outputted.

[0042]Thus, both the photodetection signal S1 which sets a time interval and is

outputted from the photodetector 21, and the photodetection signal S2 are inputted into the difference calculation circuit 23. This difference calculation circuit 23 once memorizes the inputted photodetection signals S1 and S2 to an internal memory (not shown), subsequently asks for those difference, and outputs the differential signal Ss.

[0043]By using the above-mentioned differential signal Ss also in this case, the same effect as a 1st embodiment can be acquired.

[0044]Next, drawing 3 shows the outline side shape of the surface plasmon resonance measuring device by a 3rd embodiment of this invention. In the surface plasmon resonance measuring device of this 3rd embodiment, the diameter of optical beam L after being multiplexed with the dichroic mirror 18 is expanded by the beam expander 30, and it enters into the interface 13a of the dielectric plate 13 and the metal thin film 14 in that state. Then, optical beam L irradiates with the two-dimensional field in this interface 13a.

[0045]With the dichroic mirror 20, optical beam L which carried out total internal reflection by the interface 13a is separated spectrally into the optical beam L1 of the wavelength  $\lambda_1$ , and the optical beam L2 of the wavelength  $\lambda_2$ . The optical beam L1 and the optical beam L2 are detected by the 1st two-dimensional photodetector 41 and the 2nd two-dimensional photodetector 42 which consist of a two-dimensional CCD sensor, respectively.

[0046]And both the photodetection signal S1 which the 1st two-dimensional photodetector 41 outputs also in this case, and the photodetection signal S2 which the 2nd two-dimensional photodetector 42 outputs are inputted into the difference calculation circuit 43. From the inputted photodetection signals S1 and S2, this difference calculation circuit 43 asks for the difference between both the signals S1 and S2 for every signal about the same pixel (that is, related with the same position within the interface 13a), and outputs the differential signal Ss.

[0047]In the surface plasmon resonance measuring device of this 3rd embodiment, the photodetection signal S1 and S2 which the two-dimensional photodetectors 41 and 42 output, respectively What shows the dielectric constant distribution of the sample 15 in the two-dimensional field in the interface 13a with which optical beam L was irradiated, and a jam show the concentration distribution of the special material in this sample 15.

[0048]And since each signal S1 and the noise component which had ridden on S2 will be offset if it asks for the difference between such the photodetection signal S1 and the photodetection signal S2, The differential signal Ss becomes what has S/N high enough, and it becomes possible to search for the concentration distribution of the above-mentioned special material with sufficient accuracy based on this differential signal Ss.

[0049]The surface plasmon resonance measuring device of this embodiment, Carry out as above-mentioned and the concentration distribution of the special material in the one sample 15 is searched for, and also it can also be used in order to carry out by

summarizing the quantitative analysis of the sample held at those sensor chips using the sensor array which arranges many sensor chips in two dimensions.

[0050]Drawing 4 shows an example of such a sensor array. This sensor array 50 comes to arrange many sensor chips 51 in two dimensions, in the device of drawing 3, is changed to the sample 15, and is allotted and used on the metal thin film 14. The sensor chip 51 holds the sensing medium combined with the special material in the sample of an analysis object, for example. As combination of such special material and a sensing medium, an antigen and an antibody are mentioned, for example. In that case, based on the differential signal  $S_s$  which took the difference between the photodetection signal  $S_1$  and the photodetection signal  $S_2$ , an antigen-antibody reaction is detectable.

[0051]And since the photodetection signal  $S_1$  and  $S_2$  are supporting the two-dimensional information in the interface 13a with which optical beam  $L$  was irradiated, respectively, If the differential signal  $S_s$  corresponding to each position of many sensor chips 51 is extracted, the extracted differential signal  $S_s$  shows the information (the above-mentioned example antigen-antibody reaction) for every sensor chip 51, respectively.

[0052]And since each signal  $S_1$  and the noise component which had ridden on  $S_2$  will be offset if it asks for the difference between the photodetection signal  $S_1$  and the photodetection signal  $S_2$  also in this case,  $S/N$  will become high enough and the differential signal  $S_s$  can detect the above-mentioned antigen-antibody reaction etc. with sufficient accuracy based on this differential signal  $S_s$ .

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## DESCRIPTION OF DRAWINGS

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[Brief Description of the Drawings]

[Drawing 1]The outline side view of the surface plasmon resonance measuring device by a 1st embodiment of this invention

[Drawing 2]The outline side view of the surface plasmon resonance measuring device by a 2nd embodiment of this invention

[Drawing 3]The outline side view of the surface plasmon resonance measuring device by a 3rd embodiment of this invention

[Drawing 4]The top view of the sensor array used in the surface plasmon resonance measuring device of this invention

[Drawing 5]The graph which shows the outline relation between the optical beam incidence angle in a surface plasmon resonance measuring device, and the detection light intensity by a photodetection means

[Drawing 6]The graph which shows the outline relation between the wavelength of the optical beam in a surface plasmon resonance measuring device, and the detection light

intensity by a photodetection means

[Description of Notations]

11 Dielectric prism

12 Refractive-index matching liquid

13 Dielectric plate

13a The interface of a dielectric plate and a metal thin film

14 Metal thin film

15 Sample

16 The 1st laser light source

17 The 2nd laser light source

18 and 20 Dichroic mirror

21 The 1st photodetector

22 The 2nd photodetector

23 Difference calculation circuit

25 Drive control circuit

30 Beam expander

41 The 1st two-dimensional photodetector

42 The 2nd two-dimensional photodetector

43 Difference calculation circuit

50 Sensor array

51 Sensor chip

L1, L2, L optical beam

S1 and S2 Photodetection signal

Ss Differential signal